#### SANDIA REPORT

SAND2017-13569 Unlimited Release December 2017

## Reducing Future International Chemical and Biological Dangers

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## Reducing Future International Chemical and Biological Dangers

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#### **Abstract**

The International Biological and Chemical Threat Reduction Program at Sandia National Laboratories is developing a 15-year technology road map in support the United States Government efforts to reduce international chemical and biological dangers. In 2017, the program leadership chartered an analysis team to explore dangers in the future international chemical and biological landscape through engagements with national security experts within and beyond Sandia to gain a multidisciplinary perspective on the future. This report offers a high level landscape of future chemical and biological dangers based upon analysis of those engagements and provides support for further technology road map development.

#### **ACKNOWLEDGMENTS**

The authors are grateful to Jennifer Gaudioso, George Sanzero, and Tom Nelson for their project sponsorship and support. Additionally, we are indebted to the internal workshop participants and the external subject matter experts for their contributions to this effort. Finally, we wish to thank our fellow analysts and support staff in our respective organizations for providing workshop support, content review, and other critical feedback throughout the process.

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#### **NOMENCLATURE**

ALS Amyotrophic Lateral Sclerosis

C/B Chemical and Biological

DNA Deoxyribonucleic acid

IBCTR International Biological and Chemical Threat Reduction

R&D Research and Development

RNA Ribonucleic acid

SME Subject Matter Expert

U.S. United States

USG United States Government

#### 1 BACKGROUND

The International Biological and Chemical Threat Reduction (IBCTR) Program at Sandia National Laboratories (Sandia) is developing a 15-year technology road map in support the United States Government (USG) efforts to reduce international chemical and biological (C/B) dangers. In 2017, the program leadership chartered an analysis team to explore dangers in the future international C/B landscape through engagements with national security experts within and beyond Sandia to gain a multidisciplinary perspective on the future. Over the course of the study, the team conducted 14 interviews, convened five workshops, and performed a literature review around four key questions:

- 1. What are the global trends, technological changes, and shifting security concerns that will likely affect international C/B security in the next 15 years?
- 2. What are the implications of evolving international C/B dangers?
- 3. What are the critical future uncertainties that could alter current trends?
- 4. What could the USG do to effectively prepare for these evolving international C/B dangers?

This summary provides an overview of high-level insights and implications from this process and is designed to help IBCTR program leadership develop a strategic context as they formulate their technology roadmap. Section 2 explores future dynamics generated from current trends, while Section 3 discusses the security implications of those trends. Section 4 discusses how the USG can effectively begin preparing for the future. Appendices A through C contain additional information on developing C/B subfields, SME interviewees, workshop participants, and literature referenced. A more detailed landscape report will be compiled in 2018.

**FUTURE DYNAMICS** 

Through the course of this inquiry a wide array of valuable observations and insights were explored by interviewees, workshop participants, and the analysis team. What emerged from these discussions was an overarching impression of profound changes occurring in international C/B risks. Reduced costs of capabilities, increased availability of materials and knowledge, and global connectivity are just part of a confluence of factors increasing the probability and consequences of significant C/B events—whether intentional or not. These expanding risks fall against a backdrop of a complex interplay of socioeconomic and technical dynamics, wherein unintended consequences including potential malicious hijacking of benevolent capabilities abound. The difficulty of mitigating these risks becomes magnified by the tremendous potential of C/B innovations to benefit human quality of life globally, and the USG will be fundamentally challenged to balance these benefits against its effort to minimize international C/B dangers.

Beyond these overarching insights, the analysis team identified relevant sets of more specific socioeconomic and technological trends, along with critical uncertainties (i.e. highly uncertain and impactful factors) that may produce unexpected dynamics and dramatically deviate outcomes from expectations.

#### 2.1 Socioeconomic Trends

Among the larger set of global trends that will shape the future, some trends (included below) are notable for their direct ties to the C/B landscape. While these trends are not new, collectively they are helping to generate a more interconnected and complex international environment—one less subject to human control. Critical uncertainties identified for these trends tend to reflect questions regarding how human systems—both social and biological—will respond to C/B events and capabilities.

- o Time constants for innovation and fabrication, distribution, detection, and attribution are compressing and outpacing governmental abilities to regulate emerging dangers
- Physical and virtual connectivity are expanding globally, altering and enabling vector delivery, disinformation, and other C/B threats
- Increasing global resource demands, climate change, migration, urbanization, and drugresistance of pathogens are escalating the frequency, potency, and geographic distribution of biological events
- o The gap in, and concentration of, wealth between affluent and impoverished individuals is increasing globally
- How may ethical norms, social preferences, economic incentives, and global wealth distribution impact—and be impacted by—the intent, function, adoption, and evolution of C/B innovations?
  - What methods of substantiation will garner trust in human experience-altering C/B innovations?
  - o How will extensive sharing of personal (e.g. genetic) data affect notions of ownership and
- How might greater non-governmental involvement in, and control over, research and development (R&D) affect international security and U.S. objectives in the international
- o How effective will safety and security entities be at identifying undesirable effects of interactions and preventing their occurrence or mitigating their consequences?

## **Notable Trends**

**Notable Trends** 

# Critical Uncertainties

#### 2.2 Technology Trends

The emergence of numerous new confluences and transformations of disciplines noted below increasingly merge science and engineering which will likely produce unprecedented C/B innovations in the next 15 years. These confluences will allow researchers to manipulate ever more fundamental elements and processes of living organisms and design them for targeted applications and optimal performance in human environments. With such capabilities in place, tremendous incentives exist for developing and distributing vast numbers of new C/B innovations and formulations. Critical uncertainties identified for these trends tend to reflect the potential for unintended consequences from innovation and/or surety efforts.

- Barriers to success in highly scientific fields are diminishing as cost for equipment and precursor materials decrease, access to the knowledge needed increases, and C/B outsourcing flourishes
- Data are being stored at unprecedented rates with increasingly more detail, specificity, and sensitivity
- Advancements in genetic sequencing and synthesis, coupled with growth in computing capabilities, are increasingly enabling synthetic biology to program living matter
- Increasing processing power, optimization capabilities, and accuracy of modeling and simulation are expanding scientific knowledge fundamental to innovations that may enable C/B dangers
- The lines between chemistry and biology are blurring as synthetic biology is enabling the production of complex chemical molecules at high quantities, purity, and at lower costs
- Synthetic biology is vastly expanding upon naturally occurring biologies into de novo design spaces that could result in organisms that disrupt electrical systems, chimeric viruses, biological computation and data storage / encryption, and/or organisms that target inorganic infrastructure
- o Innovations arising from the confluence of evolving fields (e.g. artificial intelligence, advanced manufacturing, neuroscience, etc.) with the C/B arena are: enabling scientific knowledge acquisition (e.g. genome-to-phenotype correlations), increasing the efficiency of processes and systems (e.g. 3-D printing of countermeasures), facilitating advanced targeting and delivery (e.g. nano-bot drug delivery), and contributing to the execution of the traditional biodefense pillars
- Human modification and augmentation are expanding human capabilities and increasingly seeking to enable effective human function in previously inhospitable environments
- How quickly will the specialized skills needed to implement these technologies and techniques diffuse into common practice or automation?
- O How will C/B technologies alter our notions of being human? And how might these altered notions impact human behaviors and systems?
- What unforeseen vulnerabilities are being introduced to organic systems through intentional genetic alterations, and will they result in massive disruptions?
- How resilient will human systems and technologies be in cases of complete failure to prevent a significant C/B-based event?

# Notable Security Implications

#### 3 SECURITY IMPLICATIONS AND STRATEGIC CHALLENGES

Based upon the current trends and critical uncertainties in the C/B landscape, the analysis team extracted security implications of these changes to international security and security providers, along with the strategic challenges the future dynamics reflect.

#### 3.1 Security Implications

Interdependency between species, balance in resources, and exogenous factors all shaped the biological systems present today, and current scientific knowledge is insufficient to understand all of the dynamics. Although we have altered ecosystems in the past (non-native species introduction, selective breeding, etc.), evolving capabilities to genetically engineer exotic / chimerical organisms for specific outcomes stimulates the underlying dynamics in novel ways. These engineered biological systems will eventually adapt, reproduce, and grow independently of the initial engineered outcome as they are influenced by the same forces of natural selection (and exogenous factors) that rejected over 99% of all species that have ever existed (Novacek 2014). Many of the advancements in the C/B arena rely on this manipulation, thus fundamentally expanding the types of imminent C/B dangers beyond traditional biodefense with a human focus.

While C/B capabilities are evolving dramatically, characterization of future security concerns will likely not differ greatly from contemporary ones. Overall these concerns will consist of intentional events (including state bioweapons, bioterror, and biocrime) and unintentional events (including accidents, natural outbreaks, and unintended consequences and use). However, the opportunities for intentional C/B events—by both state and non-state actors—are growing through innovations, illicit virtual markets, and outsourcing. Given the evolving threats and motivational ambiguities for nefarious C/B use, attribution will become increasingly important to (1) decipher intentional from unintentional events and (2) identify any altered dynamics resulting from engineered biological systems. The growing global role of non-state entities (including NGOs and multinational corporations) further suggests that their future role in generating and preventing C/B dangers may equal that of nation-states, especially if a USG leadership void allows gaps in international coordination, ethics, and surety gaps to continue.

- Growing global connectivity may blur distinctions between domestic and international C/B threats
- o C/B challenges of greatest significance may be those produced by confluences of technologies and systems and not by specific technologies and capabilities
- Global C/B security mission may evolve to a surety challenge that includes health and safety
- o Biotechnological innovations may enhance the potential for states (and possibly non-state entities) to develop bioweapons for use as effective and targeted strategic weaponry
- Greater availability of low-cost and/or low tech capabilities may cause non-attributed and misattributed C/B events to increase
- Widespread genetic modification in the future—flora, fauna, and human—may increase the susceptibility to existing and previously mitigated pathogens
- C/B landscape may evolve from agent-based threats to capability-based security challenges
- o C/B threats may put wide ranges of organisms, systems, materials, processes, and behaviors beyond physical human conditions at risk
- Nefarious actors may increasingly augment activities with novel C/B applications (e.g. bioransom)

Strategic Challenges

The insights above reflect a global need for new frameworks and approaches for this environment, and demonstrate that many future challenges will arise from C/B capabilities placing pressure upon existing cultural norms and values, economic incentives for innovation, and regulatory mechanisms—and not from not technical challenges per se.

#### 3.2 Strategic Challenges

The above security implications and future dynamics reveal the five overarching strategic challenges noted below that currently inhibit creating global assured preparedness against C/B dangers. While solving these challenges will not be sufficient for mitigating C/B dangers, addressing them will be necessary to effectively manage the risks and complexity of the future landscape.

- There is insufficient global assertion and consolidation of visions and leadership guiding approaches to surety risks, ethical challenges, and identifying unintended consequences
- Many approaches to C/B danger reduction reveal a human-centric consequence bias that overlook the potential dangers to (and human impact from) other organisms, materials, and systems
- On a global basis, incentive structures and policymaking priorities tend to encourage reactive measures over proactive surety and consequence mitigation
- O Hyper specialization of professions and research is limiting the ability to recognize or comprehend the complex dynamics of C/B innovation
- C/B innovation is increasingly endangering the ability of science to recognize and understand unintended consequences to natural systems and organisms in the absence of sufficient baselines

#### 4 PREPARING FOR THE FUTURE

The successful reduction of international C/B dangers in the next 15 years will likely depend upon a more assertive U.S. leadership role internationally. To this end, the USG should undertake the transformative organizational and leadership measures and game-changing R&D measures listed below. Both types of measures would generate a future where USG actions would shape the international community to be more proactive, anticipatory, agile, informed, cooperative, and rapidly responsive to C/B dangers—thereby building a global resilience to threats.

- Facilitate an international articulation and execution of a global vision for C/B surety establishing roadmaps, bioethics, education mechanisms, and cooperative institutions that integrates both state and non-state entities and perspectives
- Acknowledge and prepare for the full spectrum of C/B dangers using risk-based analyses that expand beyond direct effects to humans
- Prioritize multipurpose/multiuse solutions and multi-/inter-disciplinary capabilities to better understand, anticipate, and mitigate unintended consequences of emerging C/B dangers
- Pursue rapidly deployable, simple, broad spectrum engineered controls and countermeasures, including multivalent vaccines, phylum level vaccines, and immune response specific capabilities
- Develop real-time, multi-data stream integrated surveillance and monitoring of animal health, human health, and emerging pathogens in accordance with privacy protections and legal frameworks
- Begin developing a comprehensive archival scientific collection of chemical, viral, and bacterial agents and genetic material (before widespread genetically engineered system changes occur)
- Pursue genome protection that safeguard the genetic information of individuals and populations as well as genes themselves from unintended and destructive alterations

### APPENDIX A. RAPIDLY DEVELOPING SUBFIELDS THAT INFLUENCE C/B DANGERS

As the future unfolds, the following sub-fields, outlined at a high level) will expand the quality, type, and degree of C/B dangers. While much of the potential highlighted in these capabilities may lie beyond the 15-year timeframe of this report, they are nonetheless future capabilities that Sandia program leadership should consider in their roadmap development. Additionally, key enabling advancements in other fields that could strongly influence the direction of C/B dangers are highlighted. The confluence of these disciplines allows for a wide range of beneficial and hazardous applications; some potential applications are discussed.

#### **Notable C/B Subfields**

Synthetic Biology "combines the investigative nature of biology with the constructive nature of engineering" to "make living matter fully programmable" (Andrianantoandro et al. 2006; Purnick and Weiss 2009). Synthetic biology includes using genetics to design and synthesize useful organisms, biomolecules, chemistries, materials, cryptographies, and platforms. Synthetic biologic systems will no longer be limited to the evolutionarily selected design space amplifying the potential opportunity space for de novo designs with unquantified and unknown interactions in the natural environment. This subfield is itself very large; a few of the most relevant aspects/embodiments are described below.

Genetics encompasses reading, modifying, and synthesis of genetic material (genome, epigenetics, proteomics, microbiome) to understand and manipulate genome-to-phenotype correlation. Although there are many significant challenges (moving to in vivo from in vitro, the role of epigenetics, complexity inherent in phenotype expression, etc.), the progress in the field since the 1990's has been extensive resulting in fast and cheap sequencing as well as accurate and cheap editing. In the future, genome editing technologies (e.g., CRISPR-Cas) and delivery platforms will likely allow humans to edit the genome at specific locations to affect desired changes with increasing fidelity (Cong et al. 2013; Ma et al. 2017; Cyranoski and Reardon 2017). This capability offers significant advances which may hold strong benefits for humans including: curing genetic diseases like ALS, and enhancing the capabilities of humans (cut resistant skin, life-extension, etc.). In contrast, this realm of engineering biology also opens the door to dangerous developments, including: chimeric viruses capable of triggering multiple infections at once (or remaining dormant until a particular trigger is released), and a continuum of targeting capabilities from an individual to an entire population with a wide spectrum of desired effects from impairment to death. This capability also expands beyond human centric uses; naturally occurring organisms with specialized properties can be newly designed to effect significant damage. For instance, lithotrophs or the microorganisms currently affecting the nation's fighter jets (Tracy 2016) could be enhanced to more efficiently degrade inorganic infrastructure.

**Bioinformatics** combines computer science, statistics, mathematics, and engineering to analyze and interpret biological data. This field is necessary for genome-to-phenotype correlation, and is a sub-set of the application of data analytics to biology. **In the future**, as computational power and the data available for analysis increase, this area will deepen the relational understanding between coding (DNA, RNA, proteins) and expression. The increased correlative power will enable the broader area of synthetic biology.

Chemical Synthesis is the production of desired chemicals either through natural physiological processes or through controlled reactions. Traditionally chemical synthesis has been relegated to the field of synthetic chemistry, however the production of stereochemically pure small molecules for industrial needs (medical, agriculture, material, etc.) has been increasingly met through the techniques of synthetic biology (Carothers, Goler, and Keasling 2009; Smanski et al. 2016). In the future, advances in genetics (needed because production pathways comprise dozens of genes), control over catalytic reactions, and high-throughput system assembly will enable production of hundreds of thousands of complex chemical molecules at higher quantities, purity, and at lower cost (Carothers, Goler, and Keasling 2009; Smanski et al. 2016). Given the broad application space, the intended and unintended consequences of this development range from impacts to food production, to contamination of medical fluids, to the development of de novo or existing chemical warfare precursors or final products through nontraditional less easily monitored methods.

**Biocircuitry** involves arranging synthesized biology into configurations that allow for penetration into traditionally inorganic spheres of computing, communication, electromagnetic spectrum expression, etc. Currently there is increased interest in biological 'electronics' including biological voltage production and transmission (e.g., human heart, electric eel, modified E. coli (Pearlman 2016)) and biological capabilities in the electromagnetic spectrum (e.g. bacteria generating radio waves (Widom et al. 2011), augmentation with nanoparticles to emit x-rays (Krishnamurthy et al. 2015)). The ability to release and react to stimuli enable engineered biologic systems to act as logic gates, to transform and signal the transformation of protein configurations, and to reproduce these engineered configurations and capabilities. This thus offers novel opportunities to have biologically based computation, storage of information, and to also dramatically increase cryptographies to ensure secure data and algorithms (Church, Gao, and Kosuri 2012). In the future, given these inherent, augmented, and de novo designed capabilities, new biological organisms may be developed to disrupt the electrical integrity of systems. These self-replicating "electric viruses" could infect the control systems of civilian or defense applications and could be very difficult to detect or disinfect. These engineered biologic systems may also become the foundation of communication systems, computers, and information storage.

Tissue Engineering involves developing methods to encourage tissue growth on (biodegradable) lattices (Gao et al. 2016; Wang et al. 2016), 3-D printing new organs (printed directly using scaffolding (biomimicry), arrange via self-assemble by controlling ambient environment, or start with the smallest structural and functional component and let it grow (Murphy and Atala 2014)), and altering genetics to achieve "unnatural" properties. With the printing techniques and currently available materials, there are still challenges in achieving the desired 3D shapes, mechanical and structural properties, bioactivity, and degradation properties for many applications (Murphy and Atala 2014; Guvendiren et al. 2016; Wang et al. 2016). Further, the ability to develop the infrastructure (blood vessels or nerves) needed to maintain health and bioactivity of the printed material still needs significant research (Murphy and Atala 2014). In the future, many of these challenges will be overcome and enhancing tissue and organ capabilities

<sup>\*</sup> DARPA has a 'RadioBio' call specifically looking for biological organisms that may be able to generate and/or respond to electromagnetic radiation

beyond natural levels (e.g., night vision, resistance to radiation, increased pain tolerance, etc.) may be of particular interest to national security (Zhang 2015).

Wearables and Implantables are augmenting technologies that expand naturally occurring capabilities or can monitor functionality of natural systems. Limitations on biomedical implants and wearables relate not only to biocompatibility but also to the ability to make conducting materials and their substrates that are elastic, strong, and conform and adhere to organic biological shapes with various properties (Jarchum 2017; Tingley 2013). In the future, devices worn on the body will enhance human capabilities including physical strength (Cornwall 2015). Further, glasses (Levy 2017) and contact lenses (S. S. Kim et al. 2007; Ho et al. 2008) may provide information directly to the eyes. Flexible, adhesive technologies attached directly to the skin will enable both communication/control (Kao et al. 2016) as well as continuous sensing/monitoring of human vitals (D.-H. Kim et al. 2011; Koh et al. 2016) offering the potential to further human performance monitoring and optimization. Eventually, mind-mind (Rao et al. 2014) and mind-machine (Reuters Staff 2015) interfaces may enable humans to wirelessly communicate with each other and with their devices.

**Biomimicry** involves non-biological/materials-based solutions conceptualized from discoveries of biological systems, properties, and phenomena (e.g., nano-bots mimicking organisms (Huang et al. 2016), neural network algorithms, genetic optimization algorithms, folding of organelles or proteins (Colapinto 2014)). **In the future**, as deeper scientific understanding of complex biological systems is found, inspiration for *in vivo* delivery mechanisms, machine learning techniques, self-assembly, and other areas are expected. Although the potential impact of this field may extend far beyond C/B dangers, particular applications, like the development of advanced mobile micromachines mimicking the flagellar mechanisms used to propel organism in liquids (Huang et al. 2016), offer difficult to detect and highly controllable delivery mechanisms.

**Natural pathogens** are disease causing bacteria, virus, and microorganisms that evolve over time and when subject to differing environmental conditions. Comprehensive knowledge of existing pathogens is lacking; PREDICT<sup>†</sup> was created in 2009 to improve global detection and discovery of zoonotic viruses of pandemic potential and has found nearly 1,000 new viruses (Doucleff and Greenhalgh 2017). Perceptions of vaccinations have also placed herd immunity at risk in the US (Parker, Blackburn, and Natsios 2017). *In the future*, not only will the environment have changed but potentially human genetic make-up will be altered; hence susceptibility to new and existing diseases will rise.

#### Additional R&D Fields

Advancements in any, or all, of the following fields can strongly influence the development of the subfields above.

**Artificial Intelligence**: Combining the capabilities of artificial intelligence with biological and chemical arena results in multi-dimensional impacts. Combining computing, machine learning, and data analytics with a target towards biological and chemical spaces allows for *de novo* and highly effective design options (e.g. toxins, chemicals, pathogens, etc.) that are potentially disruptive and hazardous as much as they are beneficial (e.g. drugs, vaccines, etc.). Artificial intelligence could also dramatically increase

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<sup>†</sup> http://www.vetmed.ucdavis.edu/ohi/predict/index.cfm

fundamental knowledge in biologic systems by enhancing the efficiency and effectiveness of bioinformatics for instance. However, these gains also expose vulnerabilities as we can see from the work of Lippert (Lippert et al. 2017) in which genetic sequences were used to construct faces with 80% accuracy. A last highlighted dimension would be to the pillars of biodefense; employing artificial intelligence in surveillance, logistical, and anticipatory work could increase the efficiency, scope, and efficacy of these areas.

**Computing**: As processing power increases, the ability to efficiently use optimization and search algorithms will also increase. Modeling and simulation capabilities will increase further refining knowledge and hence the set of possible solutions to a given challenge. Combining increased processing power with simulation capabilities will lead to new breakthroughs in many scientific fields directly enabling the innovation space encompassing the C/B arena.

**Cyber:** As more of the population in the world, market places, and information transition to the internet, so does the potential for sharing, hacking, and selling. The web, and in particular the dark web, offers a mechanism for nefarious actors to share sensitive information and to sell potentially dangerous materials. Understanding how and what to regulate (information, materials, methodologies, sequences, etc.) is not straightforward due to the dual-use capabilities of many of the innovations, and even with the knowledge of what to regulate cyber capabilities dramatically enhance alternative mechanisms to circumvent these regulations.

**Data Analytics:** Data will continue to be stored in vast amounts with increasingly more detail and specificity. Ownership of this data, access to this data, and security of this data will elevate in importance as population based genomics will enable more advanced genome-to-phenotype correlation, new protein design, and more powerful and personalized treatment modalities. Proxy identifiers (e.g. increased Sudafed purchases) will be increasingly important in confirming, anticipating, and localizing outbreaks. Unique anonymized datasets will be cross-correlated to unveil identification of individuals, more complete genetic sequences, and other intentionally concealed or compartmentalized data.

**Materials Science**: Biological materials offer the potential for properties that are difficult to achieve with synthetic chemistry, including the ability to rapidly grow, self-repair, expand the strength and fracture toughness range, and adapt to the environment. Basic materials science combined with synthetic biology can increase yield, decrease cost, and expand the characteristics of available materials. Non-traditional application of these materials (e.g. as the outer coating of buildings) also potentially introduces new vulnerabilities to pathogens or toxins.

**Advanced Manufacturing**: Advances in additive manufacturing to enable faster production times, multiple inks within the same apparatus, as well as cheaper and smaller footprints will facilitate breakthroughs that will impact the C/B arena. Point of use printing could offer many responses to an outbreak: healthy replacement organs (Murphy and Atala 2014), needed countermeasures from drugs to equipment (Mearian 2016), or transmission reduction measures like keeping people home by printing food sources from basic constituent material (Dance 2017). This will also allow for the skirting of potential regulations designed to limit the access to equipment needed to generate a C/B danger.

**Internet of Things**: The ubiquitous connectedness of everyday objects to cyber structures that are storing data allow for an unprecedented opportunity to correlate behavior to neuro-cognitive models. The specific knowledge of peoples' patterns, locations, and habits can be used for advanced targeting.

**Medicine**: Understanding of genetic diseases, pathogens, cellular function through to hierarchical organ function, and the influence of toxins and materials in the environment on human health will continue to increase. The honing of medical practices to the individual person based on their genetics and environment will continue. This increased knowledge, simultaneously at the population and personal scales, will offer increased treatments as well as new pathways for disruption.

**Neuroscience**: Capabilities to both understand and control neurological processes of thought, emotion, and behavior will continue to increase (DiEuliis and Giordano 2017). Agents that affect the neural system are not confined solely to toxins, and as this field increases in capabilities, so will the nefarious employment of its' developments. Affecting the cognitive and emotional states of decision makers, the general populous, or key leaders offers a dangerous employment of this science and certainly falls within the emerging C/B dangers.

**Nanotechnology**: The development of nanodevices, nanoparticles, nanoscale phenomena, and nanotools for medical and biological purposes combines the field of nanotechnology with the C/B arena. Advanced delivery mechanisms for drugs, monitoring of cellular functions, regenerative medicine, and manipulation of molecular processes are all bolstered in this confluence.

#### **APPENDIX B. INTERVIEWEES**

The primary source of data for this report were collected through a series of subject matter expert interviews in the fields of chemical and biological security and safety, as well as through a series of internal workshops at Sandia National Laboratories. The table below provide information on the interviews the analysis team conducted.

Table B-1. Subject Matter Experts Interviewed

Name	Affiliation	Date Interviewed
Andy Weber	Nuclear, Chemical & Biological Defense Programs	March 31, 2017
Anup Singh	Sandia National Laboratories	March 23, 2017
Beth Cameron	National Security Council / Nuclear Threat Initiative	April 6, 2017
Dennis Carroll	United States Agency for International Development	March 23, 2017
Jerry Epstein	Office of Science and Technology Policy	March 21, 2017
Jim Carney	Sandia National Laboratories	March 24, 2017
Joe Ballard	Organisation for the Prohibition of Chemical Weapons	April 3, 2017
Jonathan Forman	Organisation for the Prohibition of Chemical Weapons	April 12, 2017
Juan Lubroth	Food and Agriculture Organization of the United Nations	April 5, 2017
Kathleen Vogel	University of Maryland	October 19, 2017
Maureen Bartee	Centers for Disease Control and Prevention's Center for Global Health	April 6, 2017
Sean Kirkpatrick	United States Strategic Command / Defense Intelligence Agency	March 16, 2017
Seth Carus	National Defense University	March 29, 2017
Tammy Beckham	Kansas State University	March 22, 2017

#### APPENDIX C. BIBLIOGRAPHY

The following publications either directly or indirectly informed the observations and findings of this report. For more information, please contact the authors.

- Alibek, Ken. Biohazard. Random House, 2008.
- Andrianantoandro, Ernesto, Subhayu Basu, David K. Karig, and Ron Weiss. 2006. "Synthetic Biology: New Engineering Rules for an Emerging Discipline." *Molecular Systems Biology* 2 (1): 2006.0028. doi:10.1038/msb4100073.
- Bernard, K. W., 2013. Health and national security: A contemporary collision of cultures. *Biosecurity and bioterrorism: biodefense strategy, practice, and science*, 11(2), 157-162.
- Boddie, C., Watson, M., Ackerman, G., & Gronvall, G. K., 2015. Assessing the bioweapons threat. *Science*, *349*(6250), 792-793
- Booker, K., Google Ventures and the Search for Immortality, in Bloomberg Markets. 2015.
- Brain Stimulation Therapies. NIH National Institute of Mental Health 2016 June; Available from: https://www.nimh.nih.gov/health/topics/brain-stimulation-therapies/brain-stimulation-therapies.shtml part \_152881.
- Carothers, James M, Jonathan A Goler, and Jay D Keasling. 2009. "Chemical Synthesis Using Synthetic Biology." *Current Opinion in Biotechnology*, Protein technologies / Systems and synthetic biology, 20 (4): 498–503. doi:10.1016/j.copbio.2009.08.001.
- Church, George M., Yuan Gao, and Sriram Kosuri. 2012. "Next-Generation Digital Information Storage in DNA." *Science*, August, 1226355. doi:10.1126/science.1226355.
- Colapinto, J., 2014. Material Question. The New Yorker.
- Cong, Le, F. Ann Ran, David Cox, Shuailiang Lin, Robert Barretto, Naomi Habib, Patrick D. Hsu, et al. 2013. "Multiplex Genome Engineering Using CRISPR/Cas Systems." *Science* 339 (6121): 819–23. doi:10.1126/science.1231143.
- Cornwall, Warren. 2015. "Feature: Can We Build an 'Iron Man' Suit That Gives Soldiers a Robotic Boost?" *Science*, October 15. http://www.sciencemag.org/news/2015/10/feature-can-we-build-iron-man-suit-gives-soldiers-robotic-boost.
- Covello, V. T., Peters, R. G., Wojtecki, J. G., & Hyde, R. C., 2001. Risk communication, the West Nile virus epidemic, and bioterrorism: responding to the commnication challenges posed by the intentional or unintentional release of a pathogen in an urban setting. *Journal of Urban Health*, 78(2), 382-391.
- Cronin, A. K., 2004. Terrorist motivations for chemical and biological weapons use: Placing the threat in context. *Defense & Security Analysis*, 20(4), 313-320.
- Cyranoski, David, and Sara Reardon. 2017. "Chinese Scientists Genetically Modify Human Embryos." *Nature News*. Accessed June 21. doi:10.1038/nature.2015.17378.
- Dance, Amber. 2017. "Engineering the Animal out of Animal Products." *Nature Biotechnology* 35 (8): 704–7. doi:10.1038/nbt.3933.
- DiEuliis, Diane, and James Giordano. 2017. "Why Gene Editors Like CRISPR/Cas May Be a Game-Changer for Neuroweapons." *Health Security* 15 (3): 296–302. doi:10.1089/hs.2016.0120.
- DIY CO2 Incubator Bioreactor for Mammalian Cell Culture. The Pelling Lab; Available from: <a href="http://www.pellinglab.net/diy/diyco2incubator/">http://www.pellinglab.net/diy/diyco2incubator/</a>.
- DNA Tinker Studio. 2016; Available from: <a href="https://synbiota.com/tinker\_kit">https://synbiota.com/tinker\_kit</a>.

- Doucleff, Michaeleen, and Jane Greenhalgh. 2017. "Why Killer Viruses Are On The Rise." *All Things Considered*. Naitonal Public Radio. http://www.npr.org/sections/goatsandsoda/2017/02/14/511227050/why-killer-viruses-are-on-the-rise.
- Elgan, M. Why a smart contact lens is the ultimate wearable. Computerworld 2009 May 9; Available from: <a href="http://www.computerworld.com/article/3066870/wearables/why-a-smart-contact-lens-is-the-ultimate-wearable.html">http://www.computerworld.com/article/3066870/wearables/why-a-smart-contact-lens-is-the-ultimate-wearable.html</a>.
- Fauci, A. S., Collins, F.S., 2012. Benefits and risks of influenza research: lessons learned. *Science* 336, no. 6088: 1522-1523.
- Gao, B., Yang, Q., Zhao, X., Jin, G., Ma, Y., Xu, F., 2016. 4D Bioprinting for Biomedical Applications. Trends in Biotechnology 34, 746–756. doi:10.1016/j.tibtech.2016.03.004
- Gates, B., 2017. Bill Gates: A new kind of terrorism could wipe out 30 million people in less than a year and we are not prepared. *Business Insider*. <a href="http://www.businessinsider.com/bill-gates-op-ed-bio-terrorism-epidemic-world-threat-2017-2">http://www.businessinsider.com/bill-gates-op-ed-bio-terrorism-epidemic-world-threat-2017-2</a>
- Gerstein, D. M., 2016. Can the bioweapons convention survive Crispr?. *Bulletin of the Atomic Scientists*. http://thebulletin.org/can-bioweapons-convention-survive-crispr9679
- Guvendiren, Murat, Joseph Molde, Rosane M.D. Soares, and Joachim Kohn. 2016. "Designing Biomaterials for 3D Printing." ACS Biomaterials Science & Engineering 2 (10): 1679–93. doi:10.1021/acsbiomaterials.6b00121.
- Harrington, R. This genetically modified fish is coming to a grocery store near you. Tech News 2015; Available from: <a href="http://www.businessinsider.com/fda-approves-aquadvantage-gmo-salmon-2015-11">http://www.businessinsider.com/fda-approves-aquadvantage-gmo-salmon-2015-11</a>.
- Henderson, D. A., 1999. The looming threat of bioterrorism. Science, 283(5406), 1279-1282.
- Ho, H., E. Saeedi, S. S. Kim, T. T. Shen, and B. A. Parviz. 2008. "Contact Lens with Integrated Inorganic Semiconductor Devices." In *2008 IEEE 21st International Conference on Micro Electro Mechanical Systems*, 403–6. doi:10.1109/MEMSYS.2008.4443678.
- Huang, Hen-Wei, Mahmut Selman Sakar, Andrew J. Petruska, Salvador Pané, and Bradley J. Nelson. 2016. "Soft Micromachines with Programmable Motility and Morphology." *Nature Communications* 7 (July): ncomms12263. doi:10.1038/ncomms12263.
- Jarchum, Irene. 2017. "Turning Silver Dust into Electronics." *Nature Biotechnology* 35 (8): 723–723. doi:10.1038/nbt.3939.
- Kao, Hsin-Liu (Cindy), Christian Holz, Asta Roseway, Andres Calvo, and Chris Schmandt. 2016. "DuoSkin: Rapidly Prototyping On-Skin User Interfaces Using Skin-Friendly Materials." In *Proceedings of the 2016 ACM International Symposium on Wearable Computers*, 16–23. ISWC '16. New York, NY, USA: ACM. doi:10.1145/2971763.2971777.
- Kim, Dae-Hyeong, Nanshu Lu, Rui Ma, Yun-Soung Kim, Rak-Hwan Kim, Shuodao Wang, Jian Wu, et al. 2011. "Epidermal Electronics." *Science* 333 (6044): 838–43. doi:10.1126/science.1206157.
- Kim, H. and J.S. Kim, A guide to genome engineering with programmable nucleases. Nature Reviews Genetics, 2014. 15(5): p. 321-334.
- Kim, S. S., E. Saeedi, D. R. Meldrum, and B. A. Parviz. 2007. "Self-Assembled Heterogeneous Integrated Fluorescence Detection System." In 2007 2nd IEEE International Conference on Nano/Micro Engineered and Molecular Systems, 927–31. doi:10.1109/NEMS.2007.352170.
- Kingsbury, N., 2014. High-Containment Laboratories: Recent Incidents of Biosafety Lapses. *US Government Accountability Office*.

- Koh, Ahyeon, Daeshik Kang, Yeguang Xue, Seungmin Lee, Rafal M. Pielak, Jeonghyun Kim, Taehwan Hwang, et al. 2016. "A Soft, Wearable Microfluidic Device for the Capture, Storage, and Colorimetric Sensing of Sweat." *Science Translational Medicine* 8 (366): 366ra165-366ra165. doi:10.1126/scitranslmed.aaf2593.
- Knobler, S. L., Mack, A., Mahmoud, A., & Lemon, S. M., 2005. Summary and assessment. The Threat of Pandemic Influenza: Are we ready?
- Krishnamurthy, M., M. Kundu, Kartik Bane, Amit D. Lad, Prashant Kumar Singh, Gourab Chatterjee, G. Ravindra Kumar, and Krishanu Ray. 2015. "Enhanced X-Ray Emission from Nano-Particle Doped Bacteria." *Optics Express* 23 (14): 17909–22. doi:10.1364/OE.23.017909.
- Levy, Steven. 2017. "Google Glass 2.0 Is a Startling Second Act | Backchannel." WIRED, July 18. https://www.wired.com/story/google-glass-2-is-here/.
- Leitenberg, M., 2001. Biological weapons in the twentieth century: a review and analysis. *Critical reviews in microbiology*, *27*(4), 267-320.
- Li, G.Y. and D.G. Zhang, Brain-Computer Interface Controlled Cyborg: Establishing a Functional Information Transfer Pathway from Human Brain to Cockroach Brain. Plos One, 2016. 11(3).
- Lieberman, J. I., Ridge, T. J., et al., 2015. A National Blueprint for Biodefense: Leadership and Major Reform Needed to Optimize Efforts. *Bipartisan Report of the Blue Ribbon Study Panel on Biodefense*. <a href="http://www.biodefensestudy.org/index.htm">http://www.biodefensestudy.org/index.htm</a>
- Lippert, Christoph, Riccardo Sabatini, M. Cyrus Maher, Eun Yong Kang, Seunghak Lee, Okan Arikan, Alena Harley, et al. 2017. "Identification of Individuals by Trait Prediction Using Whole-Genome Sequencing Data." *Proceedings of the National Academy of Sciences*, September, 201711125. doi:10.1073/pnas.1711125114.
- Ma, Hong, Nuria Marti-Gutierrez, Sang-Wook Park, Jun Wu, Yeonmi Lee, Keiichiro Suzuki, Amy Koski, et al. 2017. "Correction of a Pathogenic Gene Mutation in Human Embryos." *Nature* 548 (7668): 413–19. doi:10.1038/nature23305.
- Mearian, Lucas. 2016. "This Is the First 3D-Printed Drug to Win FDA Approval." *Computerworld*. March 28. http://www.computerworld.com/article/3048823/3d-printing/this-is-the-first-3d-printed-drug-to-win-fda-approval.html.
- Matheson, R. Major step for implantable drug-delivery device. MIT News 2015; Available from: <a href="http://news.mit.edu/2015/implantable-drug-delivery-microchip-device-0629">http://news.mit.edu/2015/implantable-drug-delivery-microchip-device-0629</a>.
- Maxmen, A., Politics holds back animal engineers. Nature, 2012. 490(7420).
- Meyer, M., 2013. Domesticating and democratizing science: a geography of do-it-yourself biology. *Journal of Material Culture*, 18(2), 117-134.
- Murphy, Sean V., and Anthony Atala. 2014. "3D Bioprinting of Tissues and Organs." *Nature Biotechnology* 32 (8): 773–85. doi:10.1038/nbt.2958.
- Novacek, Michael J. 2014. "Prehistory's Brilliant Future." *The New York Times*, November 8. https://www.nytimes.com/2014/11/09/opinion/sunday/prehistorys-brilliant-future.html.
- Parker, Gerald W., Christine Crudo Blackburn, and Andrew S. Natsios. 2017. "The Growing Threat of Pandemics: Enhancing Domestic and International Biosecurity." Scowcroft Institute of International Affairs: Texas A&M University. The Bush School of Government and Public Service. http://bush.tamu.edu/scowcroft/white-papers/?\_ga=2.32010298.529686534.1506627474-1674252417.1506627474.
- Parmet, W. E., & Sinha, M. S., 2017. A panic foretold: Ebola in the United States. *Critical Public Health*, 27(1), 148-155.

- Pearlman, Alex. 2016. "Lightbulb Made of Modified E. Coli Fuses Biology and Electronics." *New Scientist*, October 28. https://www.newscientist.com/article/2110839-lightbulb-made-of-modified-e-colifuses-biology-and-electronics/.
- Proudfoot, C., et al., Genome edited sheep and cattle. Transgenic Research, 2015. 24(1): p. 147-153.
- Purnick, Priscilla E. M., and Ron Weiss. 2009. "The Second Wave of Synthetic Biology: From Modules to Systems." *Nature Reviews Molecular Cell Biology* 10 (6): nrm2698. doi:10.1038/nrm2698.
- Rainbow Factory. 2016; Available from: https://synbiota.com/dna-market/6.
- Rao, Rajesh P. N., Andrea Stocco, Matthew Bryan, Devapratim Sarma, Tiffany M. Youngquist, Joseph Wu, and Chantel S. Prat. 2014. "A Direct Brain-to-Brain Interface in Humans." *PLOS ONE* 9 (11): e111332. doi:10.1371/journal.pone.0111332.
- Reardon, D.C.S. Chinese scientists genetically modify human embryos. 2015; Available from: <a href="http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378">http://www.nature.com/news/chinese-scientists-genetically-modify-human-embryos-1.17378</a>.
- Regalado, A., Building a Better Goat. MIT Technology Review, 2010.
- Reuters Staff. 2015. "Chinese Researchers Unveil Brain Powered Car." *Reuters*, December 7. https://www.reuters.com/article/us-china-brainpower-car/chinese-researchers-unveil-brainpowered-car-idUSKBN0TQ23620151207.
- Rojahn, S.Y., Monkeys Modified with Genome Editing. MIT Technology Review, 2014.
- Silverman, E., 2004. The 5 Most Pressing Ethical Issues in Biotech Medicine. *Biotechnology Healthcare*, 1(6), 41–46.
- Shobert, B., "American Biotech Start-Ups Head to China for Capital Partners", Forbes, 24 November 2014
- Smanski, Michael J., Hui Zhou, Jan Claesen, Ben Shen, Michael Fischbach, and Christopher A. Voigt. 2016. "Synthetic Biology to Access and Expand Nature's Chemical Diversity." *Nature Reviews. Microbiology* 14 (3): 135–49. doi:10.1038/nrmicro.2015.24.
- TED, Anthony Atala: Printing a human kidney, in TED2011. 2011.
- The Cost of Sequencing a Human Genome. National Human Genome Research Institute 2016 July 6; Available from: <a href="http://www.genome.gov/sequencingcosts/">http://www.genome.gov/sequencingcosts/</a>.
- The Nation Faces Multiple Challenges in Building and Maintaining Biodefense and Biosurveillance GAO-16-547T: Published: Apr 14, 2016. Publicly Released: Apr 14, 2016, http://www.gao.gov/assets/680/676548.pdf
- Tingley, Kim. 2013. "The Body Electric." *The New Yorker*, November 18. https://www.newyorker.com/magazine/2013/11/25/the-body-electric.
- Tom Deerink, M.E., Negatively stained transmission electron micrographs of dividing M. mycoides JCVI-syn1. J. Craig Venter Institute.
- Tracy, David. 2016. "Tiny Bacteria Are Eating America's Fighter Jets." *Foxtrot Alpha*. September 26. http://foxtrotalpha.jalopnik.com/tiny-bacteria-ar-eating-americas-fighter-jets-1786906441.
- Treble, A., "Chemical and Biological Weapons: Possession and Programs Past and Present", *Center for Nonproliferation Studies, Monterrey*, 2002, http://cns.miis.edu/cbw/possess.htm
- Wang, Xiaojian, Shanqing Xu, Shiwei Zhou, Wei Xu, Martin Leary, Peter Choong, M. Qian, Milan Brandt, and Yi Min Xie. 2016. "Topological Design and Additive Manufacturing of Porous Metals for Bone Scaffolds and Orthopaedic Implants: A Review." *Biomaterials* 83 (Supplement C): 127–41. doi:10.1016/j.biomaterials.2016.01.012.

- Watson, C. R., Watson, M. C., Ackerman, G., & Gronvall, G. K. (2017). Expert Views on Biological Threat Characterization for the US Government: A Delphi Study. *Risk Analysis*.
- Wheelis, M., Dando, M., 2003. Back to Bioweapons?. Bulletin of the Atomic Scientists.
- Widom, A., J. Swain, Y. N. Srivastava, and S. Sivasubramanian. 2011. "Electromagnetic Signals from Bacterial DNA." *ArXiv:1104.3113* [*Physics*], April. http://arxiv.org/abs/1104.3113.
- Young, A., 2016. CDC labs repeatedly faced secret sanctions for mishandling bioterror germs. USA Today
- Yu, Y., J. Zhang, and J. Liu, Biomedical Implementation of Liquid Metal Ink as Drawable ECG Electrode and Skin Circuit. Plos One, 2013. 8(3).
- Zhang, Sarah. 2015. "Cat Eyes and Other Radical Ideas to Re-Engineer Humans for the Future." *Gizmodo*, May 15. https://gizmodo.com/cat-eyes-and-other-radical-ideas-to-re-engineer-humans-1704511039.

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